# EUDRAGIT BASED ELECTROSPUN NANOFIBERS FOR DRUG DELIVERY APPLICATIONS

## SYNOPSIS

**OF THE Ph.D. THESIS TO BE SUBMITTED**

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**BY**

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**The thesis entitled "Eudragit Based Electrospun Nanofibers for Drug Delivery Applications" has been divided in to five chapters**

**Chapter 1:**

Electrospun nanofibers: An overview and applications in drug delivery

**Chapter 2:**

Diclofenac diethylamine loaded Eudragit nanofibers for sustained drug delivery

**Chapter 3:**

Fabrication, characterization and release studies of eugenol loaded Eudragit nanofibers

**Chapter 4:**

Studies on sustained release of 2ˈ-hydroxy-2,3-dichlorochalcone derivative from Eudragit nanofibers

**Chapter 5:** Comparative study on the release of 3-hydroxyflavone from monolithic and polymer blend nanofibers

**Chapter 5A:**

Sustained release studies on 3-hydroxyflavone loaded Eudragit nanofibers to combat inflammatory conditions

**Chapter 5B:**

Release of 3-hydroxyflavone from Eudragit/polycaprolactone blend nanofibers

## Chapter 1: Electrospun nanofibers - an overview and applications in drug delivery

Nanofibers are materials with diameters typically ranging from hundreds to a few thousand nanometers. In recent years, they have garnered significant attention from researchers due to their unique and compelling properties. Electrospun nanofibers, in particular, offer a finer pore structure and a much higher surface-area-to-volume ratio compared to conventional fibers, enabling their successful application across a wide range of fields. These include nanocatalysis; biomedical and pharmaceutical applications such as tissue engineering scaffolds, drug delivery systems, wound dressings, and biosensors; environmental and filtration technologies; energy-related applications like batteries and supercapacitors; optical and electronic devices; protective clothing and defense gear; as well as broader areas like healthcare, biotechnology, and environmental engineering [1–4]. Among these diverse applications, biomedical uses have most prominently demonstrated the transformative potential of functionalized electrospun nanofibers in recent years [2,5,6].

Electrospinning is a simple and efficient technique for fabricating nanofibers. This method, which utilizes electrostatic forces to produce fibers at the nanoscale, has gained considerable momentum in recent years. Its growing popularity is largely due to the ability to easily tailor the properties of the resulting nanofibers by adjusting various solution and processing parameters during the electrospinning process. In the conventional electrospinning, drugs can be incorporated by blending them directly into the polymer solution before spinning, or they are immobilized to the fiber surface either through physical means, such as electrostatic interactions between oppositely charged groups, or by chemical methods involving reactions with functional groups [7].

The technique of controlled drug delivery is believed to be a fast-emerging field in the area of science and contributing immensely towards the healthcare system. Such delivery systems offer several benefits over the conventional methods including decreased toxicity, improved efficacy and patient's compliance [8]. When it comes to periodontitis, topical drug administration is often preferred over systemic delivery as the former ensures the effective concentration in the affected area, continuous and efficient action in the periodontal pockets and eliminating the negative effects in systemic delivery [9]. Periodontal pockets thus offer an ideal site for localized drug delivery, allowing medications to act directly on the affected areas. In the context of periodontitis, nanofiber-based delivery systems promise localized and

sustained drug release within the intrapocket space, helping to alleviate acute inflammation [10].

Among all the polymeric biomaterials in making nanofibers, Eudragit polymers have gained special interest and are considered to be an important pharmaceutical excipient in targeted drug delivery due to their biocompatibility and availability in variety of grades with different pH-sensitive dissolution/permeation properties [11,12]. Eudragit RS100 is a cationic copolymer of poly (ethylacrylate, methyl–methacrylate and chlorotrimethyl–ammonioethyl methacrylate) and contains 4.5–6.8% of quaternary ammonium groups [13]. This class of polymers are insoluble at physiological pH values but capable of swelling as well, hence they are considered to be able candidates for the suspension of drug and its effective delivery at the localized sites [14]. The positive charge on the surface facilitates a better interaction with negatively charged drugs or cellular surface of the target tissues thereby enhancing the cellular absorption of drug-polymer complex [15]. Thus, this chapter presents the research domain and outlines the background and rationale for the proposed Ph. D. thesis.

**Research gap**

Despite their biocompatibility and tuneable properties, there are very few studies on Eudragit nanofibers—particularly Eudragit RS100, for the treatment of periodontitis. Literature surveys mainly discuss the properties and drug release behaviour of Eudragit nanofibers in other parts of the body. Therefore, there remains considerable scope to investigate their release behaviour under salivary conditions for periodontitis treatment. Furthermore, although the biological properties of DEA and eugenol are widely established, their release behaviour and kinetics have not been thoroughly investigated. Most of these bioactive molecules, including chalcones and flavones, suffer from poor aqueous solubility, which leads to limited dissolution, low absorption, reduced bioavailability, and poor *in vivo* performance. This issue can be effectively addressed by incorporating them into a polymer matrix.

Taking all these considerations into account, the following objectives have been formulated for this thesis study.

**Objectives of the proposed work**

- To fabricate the Eudragit nanofibers loaded with bioactive compounds by electrospinning method
- To characterize the Eudragit composite nanofiber mats
- To evaluate the biological activities and biocompatibility of Eudragit-drug nanofiber conjugate materials
- To study the controlled release property of drug candidates from the nanofiber matrix in salivary condition
- To compare the release behaviour of drugs from monolithic and blended polymer nanofibers

**Chapter 2: Diclofenac diethylamine loaded Eudragit nanofibers for sustained drug delivery**

The study aims to develop a drug-loaded nanofiber mats for the treatment of periodontitis using the conventional electrospinning method. In this work, a synthetic polymer, Eudragit RS100, was selected as the matrix. The mass ratio of the polymer to the drug (Diclofenac Diethylamine, DEA) was varied from 0% to 10% (specifically, 1%, 2%, 3%, 5%, and 10%). Field Emission Scanning Electron Microscopy (FESEM) analysis revealed that fiber diameter decreased upon initial drug loading. However, as the drug concentration increased, the fiber diameter subsequently increased. The DEA-loaded samples exhibited a prolonged release profile, with up to 78% release from the 10% DEA-loaded sample over 58 hours. The release data were best fitted to the Korsmeyer-Peppas model. The evaluation of the diffusion index indicated a Fickian diffusion mechanism for the 1%–3% drug-loaded samples. In contrast, the 5% and 10% loaded samples showed anomalous transport, involving a combination of diffusion and polymer erosion mechanisms. The released drug demonstrated significant *in vitro* anti-inflammatory activity, effectively inhibiting albumin denaturation up to 96.44%. Additionally, *in vitro* cell viability tests confirmed the cytocompatible nature of the nanofibers. These findings were further supported by *in vivo* cytotoxicity studies conducted using the *Drosophila melanogaster* model, which showed a survival rate of 82.20% and a climbing index of 77.02%. These results support the development of a biocomposite nanofiber mats that has proven to be an effective intrapocket drug delivery system for the treatment of periodontitis.

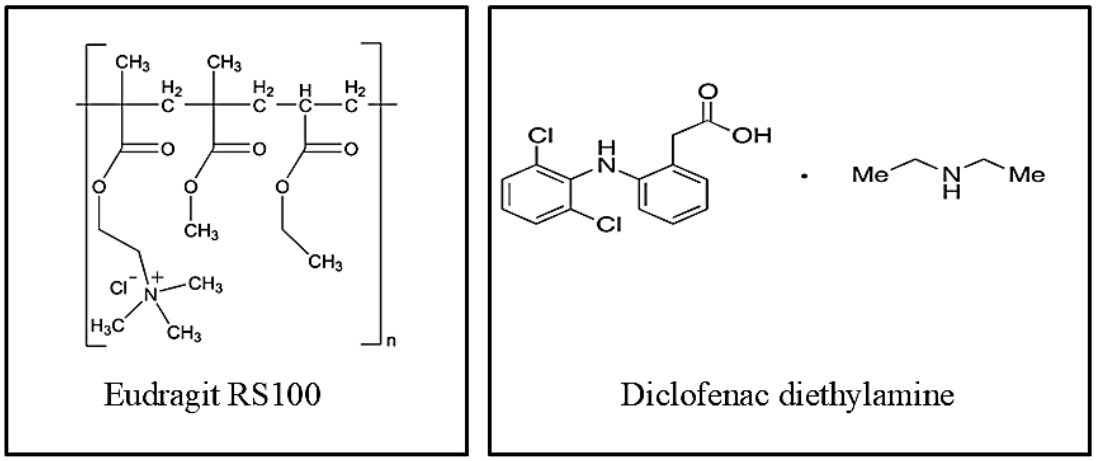


**Fig. 1**: Chemical structures of the Eudragit RS100 and DEA molecules

## Chapter 3: Fabrication, characterization and release studies of eugenol loaded Eudragit nanofibers

The current chapter focuses on the preparation of Eudragit-based nanofibers loaded with eugenol, a potential anti-inflammatory drug. The aim of this study is to explore the applicability of drug-loaded polymeric nanofibers for intrapocket drug delivery in the treatment of periodontitis. The incorporation of 1–3% eugenol into the Eudragit matrix significantly enhanced the properties of the resulting nanofibers. Field Emission Scanning Electron Microscopy (FE-SEM) revealed that the nanofibrous mat exhibited a well-branched and porous structure, with fiber diameters ranging from 261 nm to 412 nm. The presence of functional groups and the interaction between the drug and polymer through hydrogen bonding were confirmed by a shift of the absorption bands to lower wavenumbers in the FTIR spectrum. Contact angle measurements and swelling behaviour assessments demonstrated that the mat containing 3% eugenol exhibited improved surface wettability (359.17 ± 9.21%) and reduced hydrophobicity (119.80º) compared to the plain Eudragit matrix. The non-toxic nature of the developed nanofibers was confirmed through both *in vitro* cell viability assays (showing >80% viability) and *in vivo* studies using the *Drosophila melanogaster* model (with a survival rate exceeding 78%). The polymer–drug composite also exhibited excellent anti-inflammatory activity, with approximately 97% inhibition of albumin denaturation observed at a drug concentration of 12.5 µg/mL. Furthermore, the cumulative drug release of eugenol from the nanofiber mat reached 83.60 ± 2.01% for the 3% eugenol-loaded sample in the *in vitro* release study. The release data showed a high correlation coefficient ($R^2$ = 0.9681) when fitted to the

Korsmeyer–Peppas model, indicating a diffusion-controlled mechanism for prolonged drug release in a dose-dependent manner (n = 0.25, k = 10.81 $min^{-1}$).

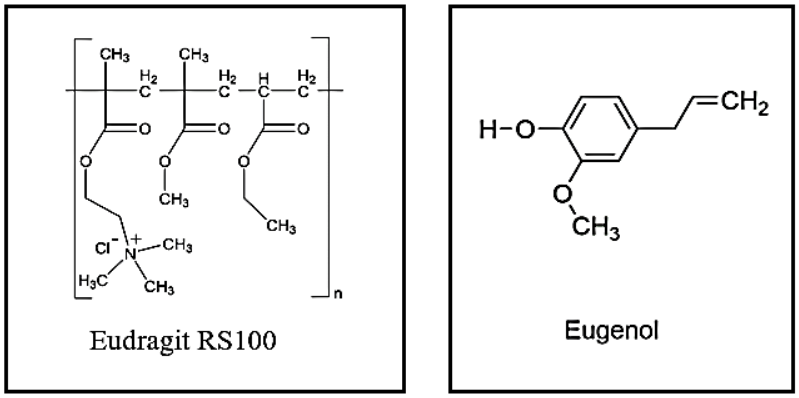


**Fig. 2**: Chemical structures of the Eudragit RS100 and eugenol molecules

## Chapter 4: Studies on sustained release of 2'-hydroxy-2,3-dichlorochalcone derivative from Eudragit nanofiber

The present work focused on investigating the release behaviour of chalcone from Eudragit-based nanofibers. A 2'-hydroxy-2,3-dichlorochalcone was synthesized via a condensation reaction between 2,3-dichlorobenzaldehyde and 2-hydroxyacetophenone. The successful incorporation of the synthesized compound into the nanofiber matrix was confirmed through Field Emission Scanning Electron Microscopy (FESEM) and UV-Visible spectroscopy analyses. The anti-inflammatory potential of the nanofiber extracts was evaluated using both the bovine serum albumin (BSA) and egg albumin denaturation methods, which demonstrated moderate to good inhibition. The cumulative drug release profile was assessed in synthetic saliva at pH 6, revealing approximately 86.81% release over a period of 64 hours. The release kinetics were best described by the Korsmeyer–Peppas model, indicating that the drug release followed a Fickian diffusion mechanism.

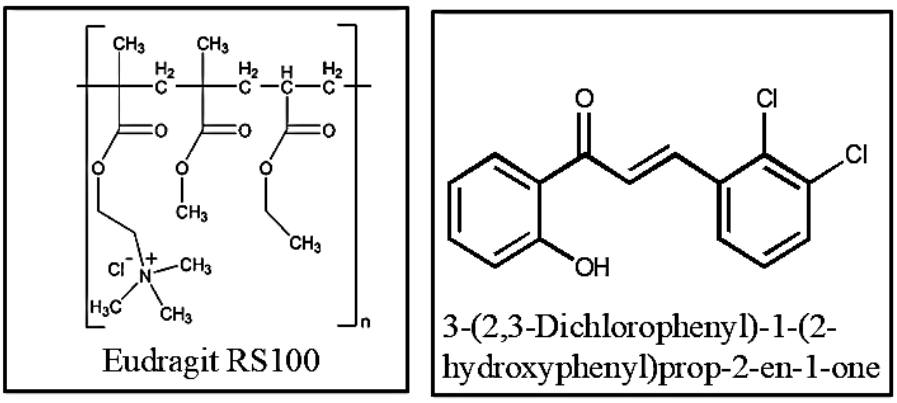

**Fig. 3**: Chemical structures of the Eudragit RS100 and 2′-hydroxy-2,3-dichlorochalcone

## Chapter 5: Comparative study on the release of 3-hydroxyflavone from monolithic and polymer blend nanofibers

### Chapter 5A: Sustained release studies on 3-hydroxyflavone loaded Eudragit nanofibers to combat inflammatory conditions

The strategy of this study involves the fabrication of Eudragit RS100 nanofibers loaded with a newly synthesized flavonoid derivative possessing potential anti-inflammatory activity, aimed at sustained drug delivery within the periodontal pocket. A polymer solution containing the bioactive compound was electrospun to form nanofibrous scaffolds, which were characterized using Field Emission Scanning Electron Microscopy (FESEM), Powder X-ray Diffraction (PXRD), Fourier Transform Infrared Spectroscopy (FTIR), UV-Visible Spectroscopy, and Thermogravimetric Analysis (TGA). The developed nanofibers exhibited bead-free, randomly oriented structures, with diameters ranging from 261 nm to 285 nm. The amorphous nature of the neat polymer was indicated by its low degree of crystallinity, while the compound-loaded samples showed a significant increase in crystallinity, suggesting a semicrystalline nature of the composite material. Surface wettability, as evaluated by apparent contact angle measurements, demonstrated a hydrophilic character, with a contact angle of $\theta = 82.8^{o}$, which decreased further with increasing drug concentration. This was accompanied by an increase in swelling capacity, favourable for enhancing cell attachment and proliferation, essential characteristics of a periodontal barrier membrane. Upon dissolution, the nanofibers exhibited a cumulative drug release of 49.26% over approximately 32 hours in an *in vitro* model. The release kinetics showed a strong correlation with the Korsmeyer–Peppas model ($R^2 = 0.9863$), indicating a diffusion-controlled mechanism. *In vitro* cell viability assays revealed a viability of greater than 90%, confirming the cytocompatibility of the developed system. Furthermore, *in vivo* biocompatibility assessed using the *Drosophila melanogaster* model showed a survival rate of 82%. The drug also demonstrated a notable anti-inflammatory effect, with >80% inhibition of albumin denaturation.

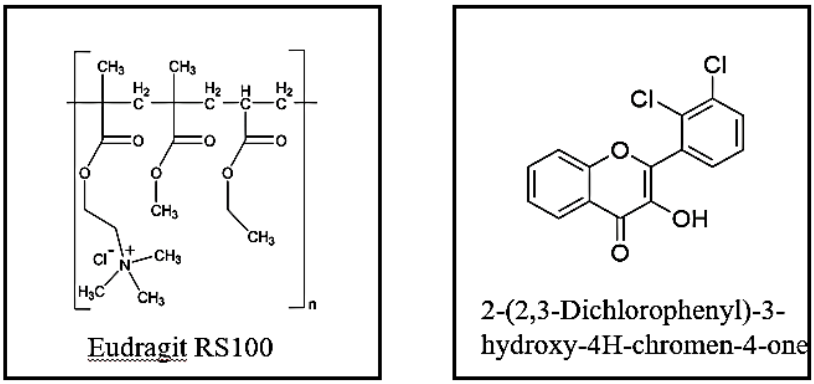


**Fig. 4**: Chemical structures of the Eudragit RS100 and 3-hydroxyflavone molecules

## Chapter 5B: Release of 3-hydroxyflavone from Eudragit/polycaprolactone blend nanofibers

**Chapter 5B** addresses the limited degradability of Eudragit nanofibers—which restricts their biomedical applications—by blending them with polycaprolactone (PCL), a biodegradable and biocompatible polymer. This matrix was loaded with previously synthesised 3-hydroxyflavone derivative. Anti-inflammatory assays (bovine and egg serum albumin methods) showed 70.27% inhibition at 50 µg/mL nanofiber extract concentration. The synthesized compound also displayed good antimicrobial activity against three Gram-positive bacteria (*Staphylococcus aureus*, *Streptococcus mutans*, *Bacillus subtilis*) and three Gram-negative bacteria (*Escherichia coli*, *Salmonella Typhi*, *Klebsiella pneumoniae*). Compared to monolithic nanofibers, the blended nanofibers had a slower release profile, achieving ~44.94% cumulative drug release over 40 hours in synthetic saliva. However, the key advantage was improved degradability, confirmed by FESEM imaging after dissolution. Overall, the developed nanofiber system demonstrated promise as an effective biodegradable biomaterial for periodontitis treatment.

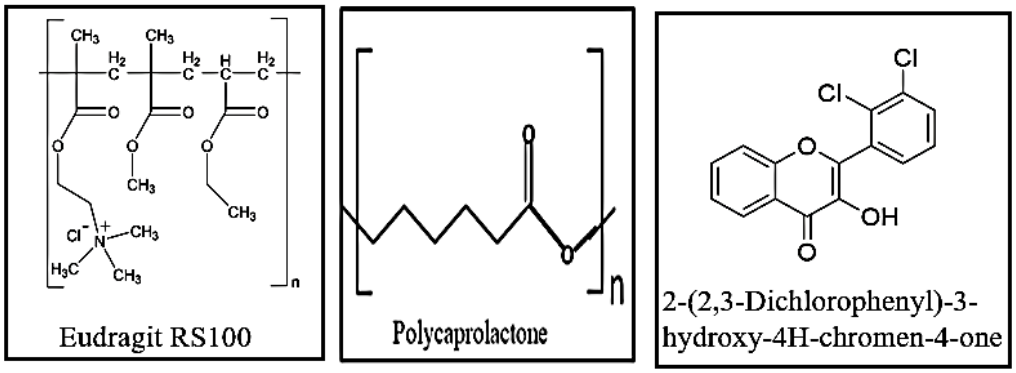


**Fig. 5:** Chemical structures of the Eudragit RS100, polycaprolactone and 3-hydroxyflavone

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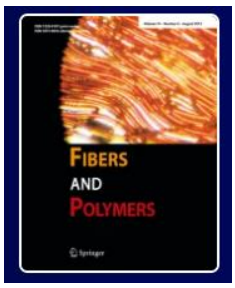
**List of Research Papers Published in Journals and Presented in Conferences**

1. **K. Shreevani**, B. Narayana, B. K. Sarojini, S. Mahammad, Suchitra, P. D. Rekha, B. S. Dayanand, S. V. Raghu. Fabrication, characterization and *in-vitro* drug release behaviour of electrospun Eudragit/eugenol nanofibrous scaffold. Fibers Polym. 25 (2024) 2817-2834. https://doi.org/10.1007/s12221-024-00622-4 (Impact Factor: 2.3)




2. **K. Shreevani**, B. Narayana, B. K. Sarojini, B. S. Dayananda, A. Ganesha, P. D. Rekha, R. A. Aziz, S. V. Raghu. Sustained release studies on 3-hydroxyflavone loaded Eudragit nanofibers to combat inflammatory conditions. J. Drug. Deliv. Sci. Technol. 106 (2025) 106677-106694. https://doi.org/10.1016/j.jddst.2025.106677 (Impact factor:4.9)

3. **K. Shreevani**, B. Narayana, B. K. Sarojini. Fabrication and characterization of eugenol-loaded Eudragit (RS100) nanofibrous mats. International Conference on Composite Materials for Environment Protection and Remediation (ICCMEPR-2024). 2024, Gram Bharati College, Ramgarh, Kaimur, Bihar, July 2-3, PP-172, 208 (Online)

4. **K. Shreevani**, B. Narayana, B. K. Sarojini, B. S. Dayananda, S. V. Raghu. Evaluation of sustained release of 3-hydroxy flavone-loaded Eudragit nanofiber for intrapocket drug delivery. National conference on Trending Novel Technologies in Pharmaceuticals (MPCON-2024), 2024. Manipal College of Pharmaceutical Sciences, Manipal, August 29-31, OP-16

5. **K. Shreevani**, B. Narayana, B. K. Sarojini, R. A. Aziz, S. V. Raghu. Diclofenac diethylamine loaded Eudragit nanofiber as a potential drug delivery system in periodontal pockets. International Conference on Polymers, Composites, Nanocomposites, and Biocomposites (ICPCNB – 2024), 2024. Mahatma Gandhi University, India, November 8 – 10, 2024, P5 (Best poster award by ACS Applied Bio Materials)

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Mahatma Gandhi University, India
November 8 – 10, 2024

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